PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

	Applicant's or agent's file reference P-INCI-X-04-0274	FOR FURTHER	RACTION	See Form PCT/IPEA/416	
	International application No. PCT/EP2004/008511	International filing d 29.07.2004	ate (day/month/year)	Priority date (day/month/year) 30.07.2003	
	International Patent Classification A61K31/4045, C07D209/08			P3/04	
	Applicant LABORATORIOS DEL DR	. ESTEVE S.A. et al.			
)	This report is the internal Authority under Article 3	tional preliminary examinatio 5 and transmitted to the appli	n report, established by cant according to Artic	y this International Preliminary Examining le 36.	
	2. This REPORT consists	of a total of 5 sheets, includir	ng this cover sheet.		
	3. This report is also accompanied by ANNEXES, comprising:				
·	a. sent to the applicant and to the International Bureau) a total of sheets, as follows:				
	sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).				
	sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.				
	sequence listing	national Bureau only) a total of and/or tables related thereto, equence Listing (see Section	in computer readable f	mber of electronic carrier(s)) , containing a orm only, as indicated in the Supplemental tive Instructions).	
280	4. This report contains indi	cations relating to the following	ng items		
)	⊠ Box No. I Basis	of the opinion			
	Box No. II Priority	·			
			egard to novelty, inven	tive step and industrial applicability	
		f unity of invention	.		
	Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement				
	☐ Box No. VI Certair	n documents cited			
	☐ Box No. VII Certair	defects in the international a	application		
	☐ Box No. VIII Certain observations on the international application				
	L) Box No. VIII Certair	observations on the internal	ional application		
	Date of submission of the demand		Date of completion	of this report	
				of this report	
,	Date of submission of the demand		Date of completion of	of this report	

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10/566094 IAP9 Rec'd PCT/PTO 27 JAN 2005

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/EP2004/008511

	Box No. I Basis of the report				
1.	With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.				
	which is the language of a tr ☐ international search (und ☐ publication of the interna	slations from the original language into the following language, ranslation furnished for the purposes of: fer Rules 12.3 and 23.1(b)) tional application (under Rule 12.4) examination (under Rules 55.2 and/or 55.3)			
2. With regard to the elements * of the international application, this report is based on <i>(replacement sheets wl have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):</i>					
	Description, Pages				
	1-92	as originally filed			
	Claims, Numbers				
	1-73	as originally filed			
ı	☐ a sequence listing and/or an	y related table(s) - see Supplemental Box Relating to Sequence Listing			
3. 1	☐ The amendments have resu☐ the description, pages☐ the claims, Nos.☐ the drawings, sheets/figs☐ the sequence listing (spe☐ any table(s) related to se	ecify):			
4. [This report has been established as if (some of) the amendments annexed to this report and listed beload not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the supplemental Box (Rule 70.2(c)). the description, pages the claims, Nos. the drawings, sheets/figs the sequence listing (specify): any table(s) related to sequence listing (specify):				
:	* If item 4 applies, so	me or all of these sheets may be marked "superseded."			

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/EP2004/008511

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

1-73

Claims No:

Inventive step (IS)

Yes: Claims

Claims No:

Claims

1-73

Industrial applicability (IA)

Yes: Claims

1-73

No:

2. Citations and explanations (Rule 70.7):

see separate sheet



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.

PCT/EP2004/008511

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

- D1: WO 03/042175 A (ESTEVE LABOR DR) 22 May 2003 (2003-05-22)
- D2: EP-A-0 815 861 (HOFFMANN LA ROCHE) 7 January 1998 (1998-01-07)
- D3: WO 02/060871 A (FLAUGH MICHAEL EDWARD; GILLIG JAMES RONALD (US); HEINZ LAWRENCE JOSEP) 8 August 2002 (2002-08-08)
- D4: US-A-3 472 870 (GOULD BARBARA E ET AL) 14 October 1969 (1969-10-14)
- D5: EP-A-0 471 609 (SANOFI SA; SANOFI PHARMA N V SA (BE)) 19 February 1992 (1992-02-19)

2. Novelty (Article 33(1) and (2)PCT)

The present application discloses compounds of formula (la-b) (see present Claims 1, 9), which are useful as 5-HT-6 modulators.

The present compounds (see Claims 1 and 9) differ from the D1 compounds on the account of the present R1 substituent, from the D2 compounds on the account of position 5 of substitution with sulfonamide moiety on the indole ring (instead of the 4-th position for the D2 compounds), from the D3 compounds on the account of the sulfonamide moiety (see Claim 1), from the D4 and D5 compounds on the account of the A substituent of the sulfonamide function (which in the present case should contain a (hetero)aromatic ring and for the D4-D5 compounds is an alkyl or alkenyl moiety). Consequently, the novelty of the present subject-matter is acknowledged.

3. Inventive step (Article 33(1) and 33(3) PCT)

The present application discloses 5-sulfonamidoindoles which are substituted on position 1 of the indole with an amino moiety or with a (hetero) cycloaliphatic ring useful as 5-HT-6 modulators.

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.

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D1, which is regarded as being the closest prior art, discloses 5-HT-6 modulators which are also sulfonamide indoles. The main difference between the present compounds and the compounds disclosed by D1 is the position of substitution with the -(CH2)n-R1moiety on the indole ring which is not in the first position(as for the present case) but in the 3-rd position of the indole ring for the D1 compounds (see present Claim 1 and the Claim 1 of D1).

The problem underlying the present invention cannot be regarded in providing further sulfonamide indoles useful to treat diseases modulated through the 5-HT-6 receptor, for the following reasons:

D3 discloses indol-5-yl esters which are 5-HT6 antagonists and are substituted in the position 1 of the indole ring with the same moieties as in the present case(see e.g. examples 23, 28, 67 of D3 and the present Claim 1).

The present general structures (Ia) differ from the compounds disclosed by D1 only through the position of substitution with -(CH2)n-R1 moiety on the indole ring (the 1-st position in the present case and the 3-rd in D1 case). D3 teaches that compounds substituted in position 1 with a cycaloaliphatic ring (see e.g. examples 23, 28, 67 of D3) are useful as 5-HT-6 modulators.

Having regard that the present compounds differ from D1 compounds only though the position of the substitution with R1 substituent on the indol ring, and that the D3 discloses 5-HT-6 ligands which bear on the nitrogen of the indole ring the same substituents as in the present case, the skilled person would have combined the teaching of D3 with the teaching of D1 in order to solve the above-mentioned problem.

The problem underlying the present application should thus be seen in providing of sulfonamide indole derivatives with unexpected or surprising effects compared to those of the closest prior art. An inventive step cannot be recognized as it is not yet shown by appropriate information, e.g. in form of experimental data, that substantially all the claimed compounds have un unexpected property or improved activity over the structurally closest prior art compounds (D1), which is attributable to the distinguishing feature of the invention.

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